REMARKS

In connection with the present Amendments, claims 1-43, 46, 48, 50, 51, 54, 56, 58, 59 were previously cancelled, claims 44, 45, 47, 49 have been cancelled, claim 52 has been amended, and claims 60 and 61 have been added. No new subject matter has been added in connection with the amendments.

In view of the above changes and the following remarks, the Applicants respectfully request reconsideration of the claims.

35 U.S.C. § 102

The Examiner states that claims 44, 45, 47, 49, 52, 53, 55 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by (i) Wright, et al., (ii) Stevenson, et al., (iii) Chen, et al. (1994) or Chen, et al. (1996).

In response, claims 44, 45, 47, 49 concerning a genetically modified cell have been cancelled. Claim 52 concerning a method of delivering an antibody to a subject mammal has been amended to specify that the claimed method of delivering an antibody to a subject mammal does not trigger an anti-idiotype response directed against the antibody in said mammal.

Support for amendment of claim 52 specifying the non-induction of an anti-idiotype response directed against said antibody in said mammal can be found on page 16 of the application (Chapter V, "Absence of Immune Response Neutralizing the Recombinant Antibody"). Amendment specifying that the transplanted cells are mammal cells is supported by the fact that all the cells cited in the examples of the present application are mammal cells, and amendment specifying that cells according to instant invention do have a long life in the mammal's organism is supported page 8, lines 3 to 9. The new claim 60 is supported on page 15, lines 4 to 7. The new claim 61 is supported on page 7, lines 5 to 7.

An invention is deemed as anticipated only if all the elements of the considered claims are disclosed in a single art reference. "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention". *Scripps Clinic & Research Foundation v. Genentech Inc.,* 18 USPQ 2d 1001-1010 (Fed. Cir. 1991).

The Examiner states that Wright, et al. disclose non-lymphoid cells, which contain heterologous polynucleotide sequences and express and secrete an antibody. Also, the Examiner states that Wright, et al. discusses the use of antibodies for therapeutic purposes. Nevertheless, the Applicants respectfully specify that Wright, et al. recite production of antibodies in nonlymphoid CHO cells in the Chapter II entitled, "*STRATEGIES FOR IN VITRO PRODUCTION OF ANTIBODIES", Sub-chapter "A. Expression Systems*", therefore teaching a person ordinary skilled in the art that antibodies once produced in nonlymphoid are subsequently purified either from cell extract or from supernatant.

Furthermore, Wright, et al. does not mention anywhere a method in which the cells above-mentioned can be grafted in a mammal's body to deliver antibodies in the blood circulation, and the Examiner's emphasis that Wright, et al. discuss the use of antibodies for therapeutic purposes, clearly indicating that the antibody can be therapeutic (page 5 of the instant Office Action). On the contrary, Wright, et al. does neither teach nor suggest the usefulness of said cells by itself for a therapeutic purposes.

Consequently, Wright, et al. does not anticipate the instant invention because they do not teach the delivery of an antibody to a subject mammal by genetically-modified transplanted cells.

In view of the foregoing, claim 52 is novel over Wright, et al. Claims 53, 55, 57, 60 and 61 are dependent from Claim 52. It thus follows that these claims are also not anticipated by Wright, et al.

Concerning Stevenson, et al., the Examiner states the document teaches that vectors coding for an antibody can be used to express the antibody in a variety of cells, including muscle cells (page 6 of the instant Office Action).

Applicants respectfully disagree. Indeed, Stevenson, et al. only teaches the production of antibody in a prokaryotic cell expressing a vector, which contains sequence coding for an antibody (see page 214: "Production of Recombinant scFv Protein"). However, Stevenson, et al. does not teach the production of antibody in a mammal cell expressing a vector, which contains sequence coding for an antibody, neither a method of delivering an antibody to a subject mammal via transplanting of a genetically modified mammal cell. Moreover, Stevenson, et al. only describes the use of a naked DNA coding for an antibody as a direct vaccine injected into muscle (see page 215: "Naked Idiotypic DNA Vaccines").

On the contrary to the present invention, Stevenson, et al. does not teach ***a method of producing antibody,*** in which cells genetically-modified are transplanted in a mammal subject.

Applicants would like to emphasize that the aim of Stevenson, et al. was to induce a strong anti-idiotype response against said antibody (See introduction page 212), for the purpose reached as described on pages 222 and 223. Consequently, Stevenson, et al. does not teach a method of delivering an antibody to a subject mammal ***without triggering an anti-idiotype response directed against said antibody in said mammal.***

In view of the foregoing, claim 52 is novel over Stevenson, et al. Claims 53, 55, 57, 60 and 61 are dependent from claim 52. It thus follows that these claims are also not anticipated by Stevenson, et al.

Concerning the two Chen, et al. documents cited by the Examiner, Applicants disagree with the statement of the Examiner that these documents anticipate the instant claimed method.

On the one hand, Chen, et al. described a human T lymphocytes transduced in vitro in order to produce intracellular and secreted Fab fragments of a neutralizing human antibody (antibody F105). However, Chen, et al. ***does not transplant the transduced*** into a mammal subject. Despite Chen, et al.'s suggested use of such a transduced T lymphocytes in gene therapy, ***not any method is described.*** In addition, as known by a person skilled in the art, the T lymphocytes used in Chen, et al. are characterized by their ***short length of life*** *in vivo*, whereas the instant claimed ***invention relies on use of long-life cells*** able to secrete antibody for a long time into a mammal subject.

On the other hand, although the Examiner states that Chen, et al. use the non-plasmocyte COS cells to demonstrate the expression of the Fab 105 fragment, Applicants respectfully argue that Chen, et al. never teaches that COS transduced cells might be **transplanted** ***in vivo*** to produce secreted antibody able to reaches blood circulation. The experiments carried-out ***in vitro*** with COS cells were done by Chen, et al. to verify that Fab 105 produced by COS cells and remaining in intracellular compartments has the ability to neutralize intracellular HIV. Nothing is indicated about the potential ability of secreted antibody, that is, if such a secreted antibody works like the original one secreted by plasmocyte. As argued by Applicants in the previous responses to Official Actions, at the time when the present application was filed, the process of secretion of antibodies appeared to be related to a specialized pathway of B lymphocytes. In view of the above-mentioned results obtained by Chen, et al. (*i.e.* production by T lymphocytes of secreted antibody capable to neutralize HIV), a person skilled in the art would indicate that cells derived from the lymphoblastoïd line (*i.e.* T and B cells) have the proteic and enzymatic machineries able to

secrete natural, and consequently correctly folded antibodies, ability which would be likened to their same origin. At the time of the filing of the present application, one skilled in the art would not use transduced COS cells to secrete in vivo antibody because skilled artisans suggested that antibody secreted by other cell lines than lymphocytes were not functional because misfolded. Moreover, Chen, et al. indicate that an HIV carrying a mutant envelope protein that usually escapes neutralization by extracellular F105 antibody (produced by plasmocytes) is neutralized by intracellular antibody present in the transduced cells, emphasizing the difference between intra- and extracellular antibodies produced via COS cells.

In view of the foregoing, the claims 52, 53, 55, 57, 60 and 61 are novel over Chen, et al.

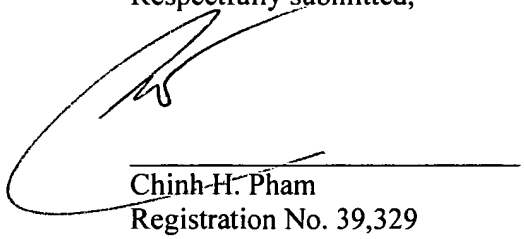
Conclusion

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. 102, (b) rejection.

Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

The Commissioner for Patents is authorized to charge any fees associated with this filing to Deposit Account No. 50-2678.

Respectfully submitted,



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